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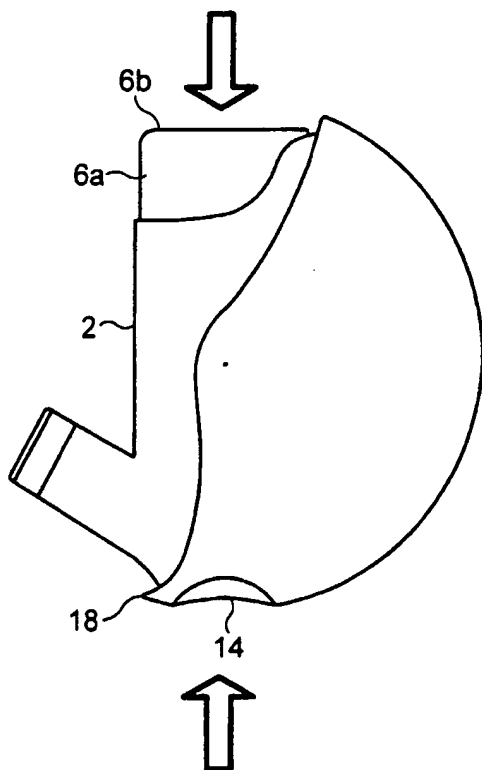
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[Continued on next page]

(54) Title: **MEDICAMENT DISPENSER**



(57) Abstract: There is provided a medicament dispenser comprising a medicament container having a dosing valve associated therewith such that medicament is dispensed in response to a force applied to an actuation point on said medicament container to depress said container relative to said valve; a body for housing said container, said body having a discharge nozzle for discharging the medicament therethrough; and a protective cover in which said body rotates between a storage position whereby said nozzle is covered and a dispensing position whereby said nozzle is exposed. The cover comprises a grip positioned such that as the medicament is dispensed, opposing forces applied to said actuation point and to said grip do not generate a turning moment urging said body to return to said storage position.

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MEDICAMENT DISPENSER

5 The present invention relates to a medicament dispenser. In particular, the present invention relates to a nasal inhalator having a protective cover.

Drugs for treating respiratory and nasal disorders are frequently administered in aerosol formulations through the mouth or nose. One widely used method for
10 dispensing such aerosol drug formulations involves formulating the drug as a suspension or a solution in a liquefied gas propellant. The suspension/solution is stored in a sealed canister capable of withstanding the pressure required to maintain the propellant as a liquid. The suspension/solution is dispersed by activation of a dose-metering valve affixed to the canister.

15

A metering valve generally comprises a metering chamber which is of a set volume and is designed to administer per actuation an accurate predetermined dose of medicament. As the suspension is forced from the canister through the dose metering valve by the high vapour pressure of the propellant, the propellant rapidly
20 vaporizes leaving a fast moving cloud of very fine particles of the drug formulation. This cloud of particles is directed into the nose or mouth of the patient by a channelling device such as a cylinder or open-ended cone. Concurrently with the activation of the aerosol dose-metering valve, the patient inhales the drug particles into the lungs or nasal cavity. Systems of dispensing drugs in this way are known as
25 "metered dose inhalers" (MDI's). See Peter Byron, Respiratory Drug Delivery, CRC Press, Boca Raton, FL (1990) for a general background on this form of therapy.

Patients often rely on medication delivered by MDI's for rapid treatment of respiratory disorders that are debilitating and in some cases even life threatening. Therefore, it
30 is essential that the prescribed dose of aerosol medication delivered to the patient consistently meet the specifications claimed by the manufacturer and comply with

the requirements of the FDA and other regulatory authorities. That is, every dose delivered from the canister must be the same within close tolerances.

Conventional metering valves for use with pressurized containers comprise a valve
5 stem coaxially slidable within a valve member defining an annular metering chamber,
and outer and inner seals operative between the respective outer and inner ends of
the valve stem and the valve member to seal the metering chamber therebetween.
The valve stem is hollow whereby in a non-dispensing position of the valve stem, the
metering chamber is connected to the container and charged with product therefrom.
10 The valve stem is movable to a dispensing position wherein the metering chamber is
isolated from the container and vented to the atmosphere for the discharge of
product. At rest, the valve can be biased towards the non-dispensing or dispensing
position by, for example, a spring, or by the internal pressure exerted by the
propellant composition.

15

In order to substantially alleviate or prevent contamination of the channelling
component that delivers the medicament to the nose or mouth, many inhalers have a
protective cover.

20 Such protective covers may take the form of an axially displaceable lid, or a lid
connected to the body of the inhaler device via a flexible connecting member.

EP-A-075548 discloses an aerosol dispensing device with a protective cover which
takes the form of a casing suspended to rotate about the body of the device.

25

However, such devices can be confusing to use, and moreover, the casing can
interfere with proper use of the dispensing device. Commonly, latching devices and
interacting locking members have to be fitted to the casing and or the body of the
device in order to prevent accidental closing of the casing during dispensing of the
30 medicament.

An object of the present invention is to provide a medicament dispenser having a cover which is urged to remain in the dispensing position during dispensing of the medicament. It is another object of the present invention to provide a device having grips for the user that serve at least three functions; firstly, the grips indicate the mode of operation of the device; secondly, the grips direct the user how to use the device; thirdly, the grips afford the user better handling of the device which ultimately ensures correct dispensing of the medicament and proper dosing.

Accordingly, in one aspect, the invention provides a medicament dispenser comprising:-

- (i) a medicament container having a dosing valve associated therewith such that medicament is dispensed in response to a force applied to an actuation point on said medicament container to depress said container relative to said valve;
 - (ii) a body for housing said container, said body having a discharge nozzle for discharging the medicament therethrough; and
 - (iii) a protective cover in which said body rotates between a storage position whereby said nozzle is covered and a dispensing position whereby said nozzle is exposed;
- wherein said cover comprises a grip positioned such that as the medicament is dispensed, opposing forces applied to said actuation point and to said grip do not generate a turning moment urging said body to return to said storage position.

As used herein the term *actuation point* typically refers to a position on the top of the medicament container and lies outside of the body housing the medicament container.

The invention thus provides a dispenser whereby the application of opposing forces to the top of the medicament container and to the grip on the cover, urges the body to remain in the dispensing position without the need for complex latching mechanisms between the body and cover. This differs from inhalers presently

available where the cover is held in the user's hand at a position towards the rear of the inhaler body and force applied to the top of the medicament container urges the body to rotate within the cover towards the storage position.

- 5 Preferably, the medicament container is an aerosol container.

Typically, the medicament dispenser takes the form of a nasal inhalator.

- 10 Preferably, the body further comprises a lip member to restrain movement of the body with respect to the cover.

Typically, the lip member restrains further onward rotation of the body in the cover after the body has rotated from the storage position to the dispensing position.

- 15 Thus, the lip member may take the form of a protrusion on the lowermost part of the body beneath the discharge nozzle. Thus, when the body is rotated with respect to the cover to the dispensing position, the lip prevents continued rotation in the same direction.

- 20 In one embodiment, the body further comprises a grip.

- Preferably, the grip is positioned at the distal side of the body which is opposite the discharge nozzle. Thus, this grip member may indicate to the user where to apply force to the body in order to rotate the body from the storage to the dispensing position.
- 25 position.

The grip on the cover and/or the body may comprise ridges, ribs, depressions or mounds.

- 30 Suitably, the grip on the cover and/or the body may be made from plastics, and/or fabric, and/or rubber.

Typically, the cover is suspended on the body on an axis transverse to a longitudinal axis through the medicament container.

- 5 Preferably, the axis is substantially central to the body and to the cover.

The cover and the body may further comprise interacting members to retain the body in a dispensing or storage position.

- 10 In another aspect, the invention provides a protective cover for use with a medicament dispenser as defined *supra*.

The invention will now be described further with reference to the accompanying drawings, in which:-

- 15 Figure 1 shows an exploded view of a body and a cover in accordance with the invention;

Figure 2 shows a schematic view of a medicament dispenser in accordance with the present invention in the storage position; and,

- Figure 3 shows a schematic view of the medicament dispenser of figure 1 in the
20 dispensing position.

Referring now to the figures, Figure 1 illustrates a body 2 and a protective cover 4 for use in a medicament dispenser of the present invention. The body 2 has an opening 6 for insertion of the medicament container 6a and a valve (not shown). The
25 discharge nozzle 8 is adjacent a protruding lip 10 for interacting with the cover 4. The body also has a grip 12.

The side view of the cover 4 illustrates the thumb grip 14 which is depressed and covered in ridges to avoid slippage.

Figure 2 illustrates the dispenser 16 once assembled. The grips 12 and 14 are visible on the body and the cover respectively. In use, a patient holds the cover 4 in one hand and pushes on grip 12 on the body in the direction of the arrow. The body 2 thus rotates within the cover 4 until the dispensing position shown in figure 3 is achieved. Once the lip 10 reaches the edge 18 of cover 4, the body is prevented from further clockwise rotation. In order to dispense the medicament, a patient places his/her thumb under grip 14 and a forefinger on top of the medicament container 6a at the actuation point 6b and squeezes to push down the container 6a relative to its associated valve (not shown) as shown by the arrows in figure 3. The forces exerted between the grip 14 and the actuation point 6b dispenses a dose of medicament and also does not create any turning moments which would urge the body to turn anti-clockwise, that is towards the storage position. Therefore, the positioning of the body and the cover remains stable in the dispensing position.

Appropriate medicaments for dispensing may be selected from, for example, analgesics, e.g., codeine, dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, e.g., diltiazem; antiallergics, e.g., cromoglycate (eg s the sodium salt), ketotifen or nedocromil (eg as the sodium salt); antiinfectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti- inflammatories, e.g., beclomethasone (eg as the dipropionate ester), fluticasone (eg as the propionate ester), flunisolide, budesonide, rofleponide, mometasone eg as the furoate ester), ciclesonide, triamcinolone (eg as the acetonide) or 6 α , 9 α -difluoro-11 β -hydroxy-16 α -methyl-3-oxo-17 α -propionyloxy-androsta-1,4-diene-17 β -carbothioic acid S-(2-oxo-tetrahydro-furan-3-yl) ester; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol (eg as free base or sulphate), salmeterol (eg as xinafoate), ephedrine, adrenaline, fenoterol (eg as hydrobromide), formoterol (eg as fumarate), isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol (eg as acetate), reproterol (eg as hydrochloride), rimiterol, terbutaline (eg as sulphate), isoetharine, tulobuterol or 4-hydroxy-7-[2-[[2-[[3-(2-phenylethoxy)propyl]sulfonyl]ethyl]amino]ethyl-2(3H)-benzothiazolone; adenosine 2a

- agonists, eg 2R,3R,4S,5R)-2-[6-Amino-2-(1S-hydroxymethyl-2-phenyl-ethylamino)-
purin-9-yl]-5-(2-ethyl-2H-tetrazol-5-yl)-tetrahydro-furan-3,4-diol (e.g. as maleate); α_4
integrin inhibitors eg (2S)-3-[4-({[4-(aminocarbonyl)-1-
piperidiny]carbonyl}oxy)phenyl]-2-(((2S)-4-methyl-2-[[2-(2-methylphenoxy)
5 acetyl]amino]pentanoyl)amino] propanoic acid (e.g as free acid or potassium salt),
diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium (eg as bromide),
tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or
prednisolone; xanthines, e.g., aminophylline, choline theophyllinate, lysine
theophyllinate or theophylline; therapeutic proteins and peptides, e.g., insulin or
10 glucagon; vaccines, diagnostics, and gene therapies. It will be clear to a person
skilled in the art that, where appropriate, the medicaments may be used in the form
of salts, (e.g., as alkali metal or amine salts or as acid addition salts) or as esters
(e.g., lower alkyl esters) or as solvates (e.g., hydrates) to optimise the activity and/or
stability of the medicament.
- 15 Preferred medicaments are selected from albuterol, salmeterol, fluticasone
propionate and beclomethasone dipropionate and salts or solvates thereof, e.g., the
sulphate of albuterol and the xinafoate of salmeterol.
- 20 Medicaments can also be delivered in combinations. Preferred formulations
containing combinations of active ingredients contain salbutamol (e.g., as the free
base or the sulphate salt) or salmeterol (e.g., as the xinafoate salt) or formoterol (eg
as the fumarate salt) in combination with an antiinflammatory steroid such as a
beclomethasone ester (e.g., the dipropionate) or a fluticasone ester (e.g., the
25 propionate) or budesonide. A particularly preferred combination is a combination of
fluticasone propionate and salmeterol, or a salt thereof (particularly the xinafoate
salt). A further combination of particular interest is budesonide and formoterol (e.g.
as the fumarate salt).
- 30 It may be appreciated that any of the parts of the inhaler which contact the
medicament suspension may be coated with materials such as fluoropolymer

materials which reduce the tendency of medicament to adhere thereto. Any movable parts may also have coatings applied thereto which enhance their desired movement characteristics. Frictional coatings may therefore be applied to enhance frictional contact and lubricants used to reduce frictional contact as necessary.

5

It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

The application of which this description and claims form part may be used as a
10 basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of features described therein. They may take the form of product, method or use claims and may include, by way of example and without limitation, one or more of the following claims:

15

Claims

1. A medicament dispenser comprising:-
 - 5 (i) a medicament container having a dosing valve associated therewith such that medicament is dispensed in response to a force applied to an actuation point on said medicament container to depress said container relative to said valve;
 - (ii) a body for housing said container, said body having a discharge nozzle for discharging the medicament therethrough; and
 - 10 (iii) a protective cover in which said body rotates between a storage position whereby said nozzle is covered and a dispensing position whereby said nozzle is exposed;wherein said cover comprises a grip positioned such that as the medicament is dispensed, opposing forces applied to said actuation point and to said grip do not
15 generate a turning moment urging said body to return to said storage position.
2. A medicament dispenser according to claim 1 wherein the medicament container is an aerosol container.
- 20 3. A medicament dispenser according to claim 1 or claim 2 in the form of a nasal inhalator.
4. A medicament dispenser according to any one of claims 1 to 3 wherein the body further comprises a lip member to restrain movement of the body with respect
25 to the cover.
5. A medicament dispenser according to any one of claims 1 to 4 wherein the body further comprises a grip.

6. A medicament dispenser according to any one of the preceding claims wherein the grip on the cover and/or the body comprises ridges, ribs, depressions or mounds.
- 5 7. A medicament dispenser according to any one of the preceding claims wherein the grip on the cover and/or the body is made from plastics, and/or fabric, and/or rubber.
8. A medicament dispenser according to any one of the preceding claims
10 wherein the cover is suspended on the body on an axis transverse to a longitudinal axis through the medicament container.
9. A medicament dispenser according to claim 8 wherein the axis is substantially central to the body and to the cover.
- 15 10. A medicament dispenser according to any one of the preceding claims wherein the cover and the body further comprise interacting members to retain the body in a dispensing or storage position.
- 20 11. A medicament dispenser substantially as described hereinabove and with reference to the accompanying drawings.
12. A protective cover for use with a medicament dispenser according to any one of the preceding claims.

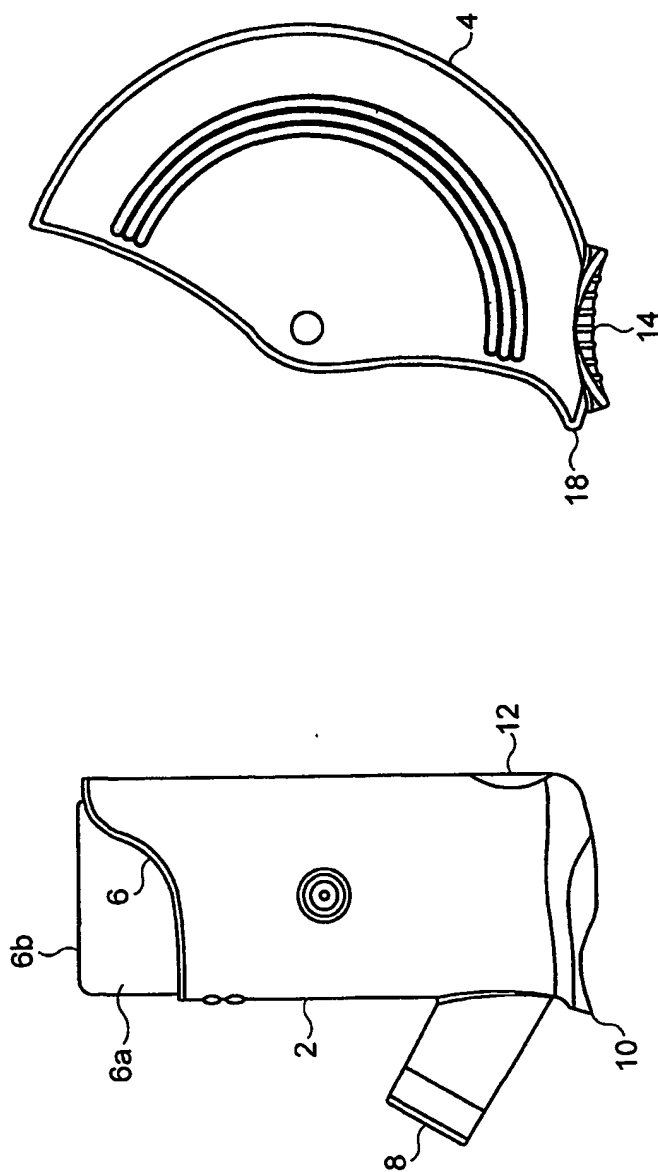


FIG. 1

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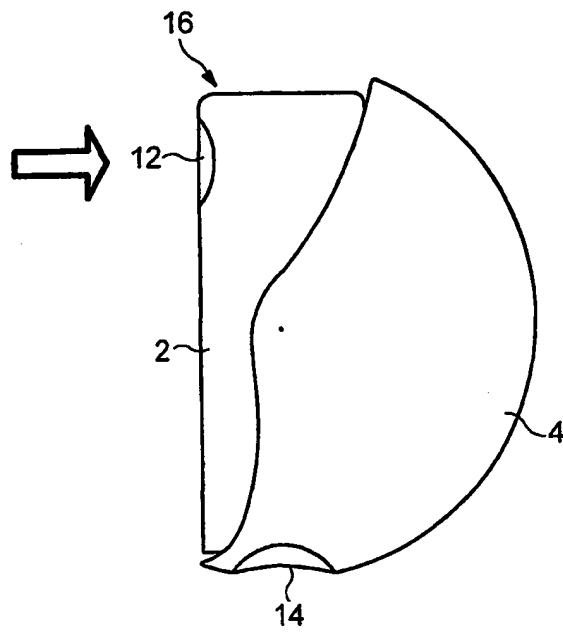


FIG. 2

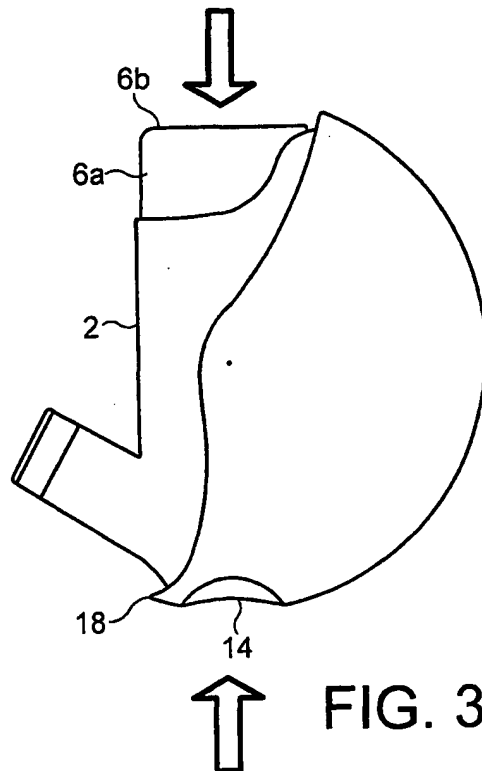


FIG. 3

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(54) Title: **MEDICAMENT DISPENSER**

(57) Abstract: There is provided a medicament dispenser comprising a medicament container having a dosing valve associated therewith such that medicament is dispensed in response to a force applied to an actuation point on said medicament container to depress said container relative to said valve; a body for housing said container, said body having a discharge nozzle for discharging the medicament therethrough; and a protective cover in which said body rotates between a storage position whereby said nozzle is covered and a dispensing position whereby said nozzle is exposed. The cover comprises a grip positioned such that as the medicament is dispensed, opposing forces applied to said actuation point and to said grip do not generate a turning moment urging said body to return to said storage position.

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A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 25405 A (ASTRA AB ;FRID PER (SE)) 27 May 1999 (1999-05-27) the whole document	1-12
A	EP 0 075 548 A (DRACO AB) 30 March 1983 (1983-03-30) cited in the application the whole document	1-12
A	EP 0 341 967 A (BESPAK PLC) 15 November 1989 (1989-11-15) abstract; figures 1,3	1-12



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Nielsen, M

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9925405	A	27-05-1999	AU 9772398 A WO 9925405 A1 US 6273084 B1	07-06-1999 27-05-1999 14-08-2001
EP 0075548	A	30-03-1983	SE 434458 B AT 20867 T AU 557695 B2 AU 8832682 A CA 1185137 A1 DE 3272156 D1 DK 413782 A ,B, EP 0075548 A2 FI 823231 A ,B, GR 78039 A1 HK 72089 A IE 53412 B1 JP 1005911 B JP 58061757 A NO 823178 A ,B, PH 23482 A SE 8105544 A SG 41889 G	30-07-1984 15-08-1986 08-01-1987 31-03-1983 09-04-1985 28-08-1986 22-03-1983 30-03-1983 22-03-1983 26-09-1984 14-09-1989 09-11-1988 01-02-1989 12-04-1983 22-03-1983 07-08-1989 21-03-1983 22-12-1989
EP 0341967	A	15-11-1989	EP 0341967 A2 US 4969578 A	15-11-1989 13-11-1990